

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
BIANCHETTI BRACCO MINOJA S.R.L.
 Attn. Banfi, Paolo
 Via Rossini, 8
 I-20122 Milano
 ITALY

**RICEVUTO IL
 RECEIVED ON**

30 SET. 2004

BIANCHETTI-BRACCO-MINOJA srl

NOTIFICATION OF TRANSMITTAL OF
 THE INTERNATIONAL SEARCH REPORT AND
 THE WRITTEN OPINION OF THE INTERNATIONAL
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year)	28/09/2004
-------------------------------------	------------

Applicant's or agent's file reference SCB 844 PCT	FOR FURTHER ACTION See paragraphs 1 and 4 below
------------------------------------------------------	-------------------------------------------------

International application No. PCT/EP2004/002185	International filing date (day/month/year) 04/03/2004
----------------------------------------------------	----------------------------------------------------------

Applicant

ISTITUTO NAZIONALE PER LO STUDIO E LA CURA DEI ...

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority	Authorized officer
-------------------------------------------------------------------	--------------------



European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Joannes Vergoosen

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SCB 844 PCT	FOR FURTHER ACTION		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/EP2004/002185	International filing date (day/month/year) 04/03/2004	(Earliest) Priority Date (day/month/year) 07/03/2003	
Applicant			

ISTITUTO NAZIONALE PER LO STUDIO E LA CURA DEI ...

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

ANAPLASTIC LYMPHOMA KINASE ASSAY, REAGENTS AND COMPOSITIONS THEREOF

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 2

☐ as suggested by the applicant.

☒ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/002185

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of Item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/002185

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-17, 19, 20

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17,19,20

ALK assay using a peptide of SEQ ID N. 1 or SEQ ID N. 2 and said peptides and related kits.

2. claim: 18

Use of compounds of formula (I) for the preparation of a medicament for the treatment of ALK-related tumors.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/002185

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/48 C07K14/72 G01N33/74 A61K31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, CHEM ABS Data, EMBASE, MEDLINE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Section Ch, Week 199325 Derwent Publications Ltd., London, GB; Class A96, AN 1993-201126 XP002249142 & JP 05 126833 A (TOSOH CORP) 21 May 1993 (1993-05-21) abstract	1-17, 19, 20
A	US 5 770 421 A (LOOK A THOMAS ET AL) 23 June 1998 (1998-06-23) the whole document	1-17, 19, 20
A	WO 95/14930 A (SADICK MICHAEL DANIEL ; GENENTECH INC (US); GODOWSKI PAUL J (US); M) 1 June 1995 (1995-06-01) the whole document	1-17, 19, 20
	----- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
 "E" earlier document but published on or after the international filing date
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
 "O" document referring to an oral disclosure, use, exhibition or other means
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

1 July 2004

Date of mailing of the international search report

28 SEP 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Gunster, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/002185

C.(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98/49317 A (PELES ELIOR ;ONRUST SUSAN (NZ); CLARY DOUGLAS (US); HUI TERANCE H) 5 November 1998 (1998-11-05) the whole document	1-17,19, 20
A	WO 95/02187 A (BARKER KAREN TRACEY ;CROMPTON MARK ROGER (GB); MARTINDALE JANE ELI) 19 January 1995 (1995-01-19) the whole document	1-17,19, 20
A	SADICK M D ET AL: "Kinase receptor activation (KIRA): A rapid and accurate alternative to end-point bioassays" JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS 1999 NETHERLANDS, vol. 19, no. 6, 1999, pages 883-891, XP002249139 ISSN: 0731-7085 the whole document	1-17,19, 20
A	TURTURRO FRANCESCO ET AL: "Model of inhibition of the NPM-ALK kinase activity by herbimycin A." CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. UNITED STATES JAN 2002, vol. 8, no. 1, January 2002 (2002-01), pages 240-245, XP002249140 ISSN: 1078-0432 the whole document	1-17,19, 20
A	MORRIS STEPHAN W ET AL: "ALK, the chromosome 2 gene locus altered by the t(2;5) in non-Hodgkin's lymphoma, encodes a novel neural receptor tyrosine kinase that is highly related to leukocyte tyrosine kinase (LTK)." ONCOGENE, vol. 14, no. 18, 1997, pages 2175-2188, XP002249141 ISSN: 0950-9232 the whole document	1-17,19, 20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/002185

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
JP 5126833	A	21-05-1993	NONE	
US 5770421	A	23-06-1998	US 5529925 A	25-06-1996
			US 6174674 B1	16-01-2001
			US 6451997 B1	17-09-2002
			US 2001021505 A1	13-09-2001
			AU 679833 B2	10-07-1997
			AU 1511695 A	19-06-1995
			CA 2177957 A1	08-06-1995
			DE 69433665 D1	06-05-2004
			EP 0731806 A1	18-09-1996
			JP 9512161 T	09-12-1997
			WO 9515331 A1	08-06-1995
WO 9514930	A	01-06-1995	US 6001621 A	14-12-1999
			AT 163231 T	15-02-1998
			AU 697142 B2	01-10-1998
			AU 1180095 A	13-06-1995
			AU 698975 B2	12-11-1998
			AU 1210895 A	13-06-1995
			CA 2175892 A1	01-06-1995
			CA 2175893 A1	01-06-1995
			DE 69408541 D1	19-03-1998
			DE 69408541 T2	06-08-1998
			DK 730740 T3	28-09-1998
			EP 0730646 A1	11-09-1996
			EP 0730740 A1	11-09-1996
			ES 2116066 T3	01-07-1998
			GR 3026430 T3	30-06-1998
			HK 1008440 A1	07-05-1999
			JP 9506250 T	24-06-1997
			JP 3442784 B2	02-09-2003
			JP 9505889 T	10-06-1997
			WO 9514776 A1	01-06-1995
			WO 9514930 A1	01-06-1995
			US 2002147325 A1	10-10-2002
			US 2003204072 A1	30-10-2003
			US 5766863 A	16-06-1998
			US 6025145 A	15-02-2000
			US 6287784 B1	11-09-2001
			US 5914237 A	22-06-1999
			US 5891650 A	06-04-1999
			US 6096527 A	01-08-2000
			US 5709858 A	20-01-1998
			US 6087144 A	11-07-2000
			US 2002137113 A1	26-09-2002
WO 9849317	A	05-11-1998	AU 7260098 A	24-11-1998
			CA 2288221 A1	05-11-1998
			EP 0979288 A2	16-02-2000
			JP 2002513289 T	08-05-2002
			US 2003073143 A1	17-04-2003
			WO 9849317 A2	05-11-1998
			US 6228641 B1	08-05-2001
			US 2002119501 A1	29-08-2002
			US 2003095970 A1	22-05-2003
			US 2003008347 A1	09-01-2003
			US 6342593 B1	29-01-2002

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/002185

Patent document cited in search report	Publication date	Patent-family member(s)	Publication date
W0 9849317	A	US 6388063 B1 US 2004087783 A1	14-05-2002 06-05-2004
W0 9502187	A	19-01-1995 AU 7081094 A W0 9502187 A1 ZA 9404983 A	06-02-1995 19-01-1995 08-01-1996

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/002185

International filing date (day/month/year)
04.03.2004

Priority date (day/month/year)
07.03.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q148, C07K14/72, G01N33/74, A61K31/00

Applicant
ISTITUTO NAZIONALE PER LO STUDIO E LA CURA DEI ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Gunster, M

Telephone No. +31 70 340-4412



WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application
PCT/EP2004/002185

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the language of the international application, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating to the invention has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application N°
PCT/EP2004/002185

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/002185

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form or do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application N
PCT/EP2004/002185

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is:
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-17,19,20

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17,19,20
	No: Claims	
Inventive step (IS)	Yes: Claims	1-17,19,20
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-17,19,20
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No

PCT/EP2004/002185

Re Item IV

The present application lacks unity of invention in the sense of Rule 13.1 and 13.2 PCT.

The application as filed is considered to lack unity of invention since its subject-matter relates not to one, but rather to two separate inventions not linked together by a common underlying inventive concept as required by Rule 13.1 and 13.2 PCT.

The claims and the inventions to which the two separate inventions relate may be grouped together as follows:

Invention 1: Claims 1-17, 19, 20

Invention 2: Claim 18

According to Rule 13.2 PCT, an international patent application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features. Special technical features are such features that define the contribution of the claimed invention over the prior art.

The contributions claimed in the present application which are allegedly made over the prior art are:

- a) the use of a peptide according to SEQ ID N. 1 or 2 as a substrate for ALK,
- b) the use of a compound according to formula (I) to produce a medicament against an ALK-related tumour.

These contributions are not so linked to form a single general inventive concept in the sense of Rule 13.1 and 13.2 PCT. The reasons therefor are the following:

The two identified inventions involve the common concept: "(identifying) modulators of ALK activity", as the sole common link. However, this concept does not define a contribution over the prior art, because it is not new (see for example US-A-5 770 421, column 14, lines 51-58). Thus, the common concept linking the alleged inventions is not new. Therefore, there is no single general inventive concept that links the claimed

inventions, which results in non-unity of invention in the sense of Rule 13.1 and 13.2 PCT.

Re Item V

The subject-matter of claims 1-17, 19 and 20 is new because ALK tyrosine kinase assays using Seq ID No 1 and 2 are not known in the prior art (Article 33(2) PCT).

The closest prior art document Turturro et al (2002) describes an assay for determining ALK autophosphorylation activity by incubating ALK with radioactive ATP and detecting labelling of ALK itself.

The additional technical feature of the application over the closest prior art is that a peptide according to SEQ ID N 1 or 2 is used to detect ALK autophosphorylation activity.

The problem that is solved by the application is the provision of a more sensitive assay. The prior art either uses a tyrosine kinase receptor itself (or an active part thereof) for determining autophosphorylation or an artificial poly Glu/Tyr peptide. There is no suggestion that a separate peptide can be used that is derived from the tyrosine kinase receptor itself. Moreover it is not known in the prior art that such peptides have a higher phosphorylation degree than the artificial poly Glu/Tyr peptide. Thus it is not obvious to use peptide 1 or 2 to achieve a more sensitive assay for ALK activity. Consequently, the subject-matter of claims 1-17, 19 and 20 involves an inventive step in the sense of Article 33(3) PCT.

The subject-matter of claims 1-17, 19 and 20 is industrially applicable in the field of molecular biology and pharmaceuticals (Article 33(4) PCT).